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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BORGEEST, CHRISTINA M	

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1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,684	MOUNTJOY ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *04 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-11,15-20,23,25,29-33 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11,15-20,23,25,29-33 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed 4 September 2007 is acknowledged. Claims 8-11, 15-18, 20, 23, 25, 29 and 33 are amended. Claim 35 is new. Claims 12-14 and 34 are cancelled. Claims 8-11, 15-20, 23, 25, 29-33 and 35 are under examination.

Rejections withdrawn

Claim Rejections - 35 USC § 112, second paragraph

The rejection of claims 8, 9-11, 14, 16, 17-20, 23, 25 and 29-31, 33-34 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps as set forth at pages 3-4 of the previous Office action mailed 3 May 2007 is withdrawn in response to Applicants' amendment of the claims to clearly recite what the method achieves and in response to Applicants' cancellation of claims 14 and 34.

Claim Rejections - 35 USC § 102

The rejection of claims 8-11, 14, 16, 17, 18, 19, 20, 23, 25, 29, 31 and 34 under 35 U.S.C. 102(b) as being anticipated by Mauri et al. (Horm Res. 1990; 34: 66-70) as set forth at pages 10-11 of the previous Office action mailed 3 May 2007 is withdrawn in response to Applicants' amendment of the claims to clearly recite all the method steps and to Applicants' cancellation of claims 14 and 34. Specifically, as Mauri et al. do not teach the measurement of α-MSH and desacetyl-α-MSH, followed by calculation of the

desacetyl-α-MSH/α-MSH ratio in order to determine that an increase in said calculated ratio above the reference ratio is indicative of an imbalance in feeding and/or weight gain pattern and/or obesity, as is now clearly recited in the claims, Mauri et al. cannot anticipate the currently claimed methods.

Claim Rejections - 35 USC § 112, first paragraph

The rejection of claims 14 and 34 under 35 U.S.C. 112, first paragraph, for scope of enablement as set forth at pages 4-11 of the previous Office action mailed 3 May 2007 is withdrawn in response to Applicants' cancellation of claims 14 and 34.

Rejection maintained/New rejection

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 8-11, 15, 16, 17-20, 23, 25 and 29-30, 32-34 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained in part. In addition, there is a new concern hereby raised by the Examiner (not necessitated by amendment), ***thus this Office action will be made non-final in order to ensure that Applicants have the opportunity to present arguments.***

Claims 8-11, 15, 16, 17-20, 23, 25 and 29-30, 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

assessing feeding and/or weight gain pattern or diagnosing obesity in an individual in need thereof, comprising measurement of α-MSH and desacetyl-α-MSH in a sample, calculating the ratio between desacetyl-α-MSH and α-MSH, and comparing the value of the ratio with a reference value, wherein a higher desacetyl-α-MSH/α-MSH ratio in the sample is indicative of an increase in feeding and/or weight gain and/or obesity, does not reasonably provide enablement for the claims as broadly recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

First, the amendment to the claims has appropriately addressed many of the concerns raised by Examiner in the Office action mailed 3 May 2007. For instance, the claims no longer recite or encompass measuring the ratio of any two melanocortin peptides. In addition, the claims now clearly recite that an increase in the calculated ratio of desacetyl-α-MSH/α-MSH predicts risk, not any ratio. Furthermore, regarding claims 15 and 33, since the parent claims recite measuring an increase in the desacetyl-α-MSH/α-MSH ratio, "the profile of response parameters" resulting from that measurement is more narrowly defined within the claim. Regarding the recitation of "measured by a biological response system" in claim 15, the claim now further recites "capable of predicting the risk of developing obesity or diagnostic of obesity, imbalance in energy homeostaisis or disturbance in feeding/weight gain patterns, which more narrowly defines the preceding phrase "biological response system".

The remaining concern of those raised in the previous Office action is the scope of what is encompassed by a sample. In claim 25, it is clear that saliva, sweat, urine, amniotic fluid, cord blood, cerebrospinal fluid, and in vitro cell, organ or tissue sample are all encompassed by the claims, however, the evidence presented by Applicants and in the literature (blood) is not commensurate in scope with the breadth of what is encompassed by the claims. For instance, although Applicants argue at p. 9, 1st paragraph that the specification must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the object truth of the statements contained therein, it is not clear how amniotic fluid or cord blood could be used in the claimed methods. Presuming that a measurement of the ratio of desacetyl-α-MSH/α-MSH could even be measured in amniotic fluid or cord blood, would an increase in the desacetyl-α-MSH/α-MSH ratio be indicative of obesity or feeding problems in the mother or the fetus? Applicants did not present evidence concerning other biological samples and it is not biologically plausible that any body tissue or fluid could be used to carry out the claimed methods.

In addition, there are new concerns not previously raised. First, claims 15 and 16 and their dependents are drawn to "predicting risk" or "assessing risk" in the alternative. Predicting and assessing risk encompass performing the claimed method on an apparently non-obese subject who may or may not develop obesity in the future in order to determine whether they will develop obesity. There are no data to support this in the specification or the literature. All of the examples are drawn to comparisons of obese and non-obese test subjects (rats), thus there is no evidence that the methods could be

used to "predict risk of obesity" in a non-obese subject. The claims encompass risk assessment in an apparently normal subject (as opposed to diagnosis of obesity in a subject suspected of being obese, for example), and there are no data to support this, thus the evidence is not commensurate in scope with the claims. Another concern are the amended claims 8, 16 (and their dependents) reciting, "...the reference ratio is indicative of an imbalance in feeding and/or weight gain pattern in the subject." Likewise, claims 15 and 16 recite a "disturbance in feeding/weight gain patterns". The use of words such as "imbalance" and "disturbance" encompasses underfeeding and weight loss, but the specification teaches that an increase in the desacetyl-α-MSH/α-MSH ratio is seen in obese mice, thus the claims are only enabled for assessing an increase in feeding and/or weight gain pattern in an individual who is already obese. One skilled in the art would expect that the ratio would change only as the condition manifests itself in a subject, not before. For instance, Nakahara et al. (Biol Psychiatry; 2007—Epub ahead of print) teach that obestatin concentrations are negatively correlated with body mass index. At the last page, last paragraph they state that "obestatin may be a useful marker of nutritional status since...it reflects adiposity and insulin resistance in humans." In addition, Yarnell et al. (J Epidimiol Community Health. 2000; 54; 344-348) teach that in men, having a high BMI (≥ 30) at age 18 was the best predictor of weight gain and obesity in middle age (see p. 347, Table 3). Nakahara et al. demonstrate that biochemical markers of feeding behavior is evident once the condition is manifested, i.e., extremely thin individuals have high levels of obestatin in relation to obese individuals (though interestingly, there was no statistically significant

difference between obestatin levels between obese and control subjects). Yarnell et al. teach that the best predictor of weight gain and obesity in middle age was a high BMI (≥ 30) at age 18. One skilled in the art would not expect that obesity could be predicted in a thin or normal weight individual with a great degree of accuracy given that 1) biochemical markers become evident once the condition has manifested itself and 2) the best predictor of later weight gain and/or obesity later in midlife was being overweight in youth. The state of the art concerning obesity and feeding/weight gain suggests to one of skill in the art that the desacetyl-α-MSH/α-MSH ratio would change only once the condition is present.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As noted above, with regard to claims 15 and 16, claim 9 is drawn to "predicting risk", which encompasses performing the claimed method on an apparently non-obese subject, who may or may not develop obesity in the future in order to determine whether they will develop obesity. ***The reasons discussed in the immediately preceding paragraph are applicable here.*** The claims encompass risk assessment in an apparently normal subject (as opposed to diagnosis of obesity in a subject suspected of being obese, for example), and for the reasons discussed above, the evidence is not commensurate in scope with the claims.

Due to the large quantity of experimentation necessary to determine how the methods could be use to "predict risk", and to determine which tissues the claimed methods could be carried out, the lack of direction/guidance presented in the specification and the absence of working examples directed to the same and the breadth of the claims which fail to recite limitations the tissues which would provide useful measurements to carry out the claimed invention, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The rejection of claim 31 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record and the following. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The reason is given in the paragraph immediately preceding this one, namely the evidence in the literature suggests that hypothalamic tissue would not be useful in the instantly claimed methods, since Harrold et al. that neither α-MSH nor POMC measured in hypothalamic tissue are indicative of obesity or energy imbalance.

Applicants argue at p. 8, 4th paragraph that the instant claims recite the use of desacetyl-α-MSH/α-MSH ratio, not the concentration or level of desacetyl-α-MSH or α-MSH. Applicants state that Harrold only measured α-MSH concentration, but the reference is silent with respect to desacetyl-α-MSH concentration; and more importantly, the Harrold reference is silent with respect to the ratio of desacetyl-α-MSH/α-MSH. Finally, Applicants note that an "unchanged concentration of α-MSH"

does not necessarily relate to a high or low ratio of desacetyl-α-MSH/α-MSH, because the ratio also depends on the concentration of desacetyl-α-MSH, which Harrold does not measure.

Applicants argue at p. 8, penultimate paragraph that they have shown in Example 3 that the hypothalamus is responsive to α-MSH and desacetyl-MSH.

Applicants argue at p. 9, 1st paragraph that the specification must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the object truth of the statements contained therein.

These arguments have been fully considered but are not found persuasive for the following reasons. First, Applicants criticize the Harrold reference for not measuring the desacetyl-α-MSH/α-MSH ratio and cite Example 3 as evidence that the hypothalamus is responsive to α-MSH and desacetyl-MSH, but Example 3 only shows that intracerebroventricular injection of α-MSH and desacetyl-MSH resulted in a diverse proteomic expression profile in the hypothalamus resulting from α-MSH and desacetyl-MSH injection. In other words, although the hypothalamus was responsive to α-MSH or desacetyl-MSH injection, as evidenced by activation of different proteins, this does not demonstrate that the α-MSH/desacetyl-MSH ratio can be measured in the hypothalamus in order to carry out the claimed methods. The teachings of Harrold et al. are not the only basis for the rejection under 35 U.S.C. and while applicants' objections to the Harrold reference are noted, the fact that α-MSH levels were unaffected by overfeeding (see p. 403, right column, last paragraph) does not provide strong evidence that an increase in the α-MSH/desacetyl-MSH ratio can be measured in the hypothalamus in order to carry out the claimed methods.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 7:00am - 1:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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